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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/888,313	06/22/2001	Ian Tomlinson	DB00002	9556

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EXAMINER	
STEELE, AMBER D	

ART UNIT	PAPER NUMBER
1639	

NOTIFICATION DATE	DELIVERY MODE
03/24/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

US_cipkop@gsk.com

Office Action Summary	Application No.	Applicant(s)	
	09/888,313	TOMLINSON ET AL.	
	Examiner	Art Unit	
	AMBER D. STEELE	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *December 11, 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *56,58-67,78-86,118 and 119* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *56, 58-67,78-86,118 and 119* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 11, 2009 has been entered.

Status of the Claims

2. The claim amendment received on June 3, 2008 amended claims 56, 58, 64, and 78; canceled claims 1-55, 69-77, and 87-117; and added new claims 118-119.

The claim amendment received on April 16, 2009 amended claims 56, 58, 62, 78, 86, and 118-119.

The claim amendment received on December 11, 2009 amended claim 56 and canceled claims 57 and 68..

Claims 56, 58-67, 78-86, and 118-119 are currently pending and under consideration.

Priority

3. The present application claims benefit of 60/246,851, filed November 8, 2000 and claims foreign priority to UK 0015443.5 filed June 23, 2000 and UK 0026099.2 filed October 25, 2000.

Invention as Claimed

4. A method for screening a first repertoire of antibody heavy chain or antibody light chain polypeptides against a second repertoire of antibody heavy chain or antibody light chain polypeptides to identify those members of the first repertoire which interact with members of the

second repertoire comprising the steps of (a) arranging the first repertoire in at least one first series of continuous lines wherein each line of said first series comprises a member of said first repertoire, (b) arranging the second repertoire in at least one second series of continuous lines wherein each line of said second series comprises a member of said second repertoire, (c) forming an array of a plurality of first and second repertoires from step a and step b wherein said first series of continuous lines from step a intersects with a plurality of said second series of continuous lines from step b wherein all members of the first repertoire are juxtaposed to all members of the second repertoire and (d) detecting an interaction between the antibody heavy chain or antibody light chain of the first and second repertoires thereby identifying those members of the first repertoire that interact with members of the second repertoire and variations thereof.

Withdrawn Rejections

5. The provisional rejection of claims 56-68, 78-86, and 118-119 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 3-23 of copending Application No. 11/413,427 due to the abandonment of the application.

Maintained Rejections

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 56, 58-67, 78-86, and 118-119 are rejected under 35 U.S.C. 103(a) as being unpatentable over Feldstein et al. U.S. Patent 6,192,168 filed April 9, 1999; Dower et al. U.S. Patent 5,427,908 issued June 27, 1995; and McCafferty et al. U.S. Patent 5,969,108 issued October 19, 1999.

For present claims 56, 62-63, 65-67, and 86, Feldstein et al. teach a microfluidic device for multianalyte interactions wherein a multimode waveguide (i.e. solid surface) is paired with a fluidic cell, flow chamber, or flow cell to perform multianalyte and multisample assays comprising flowing a first set of reagents into multiple channels (i.e. continuous lines) wherein the first set of reagents is deposited on the waveguide, then placing another set of channels perpendicular (i.e. intersection, juxtaposed) to the first set of deposited reagents and flowing a second and/or third set of reagents through the channels (i.e. applied to single support of waveguide wherein in the upper channels are utilized for containing fluid to prohibit mixing) wherein the first, second, and/or third set of reagents can interact and all members interact with each other since each channel interacts with the other channels (e.g. reagents in channel A of Figure 8b interact with each reagent in channels 1-6 from top to bottom; please refer to the entire specification particularly the abstract; Figures 7a-7b and 8a-8b; columns 3-13; claims 1-31).

For present claims 58-61 and 64, Feldstein et al. teach antibodies and antigens (i.e. heavy and light chains; please refer to the entire specification particularly column 6, lines 37-67; column 7, lines 1-7; columns 10-12; claim 7).

However, Feldstein et al. does not teach a first repertoire of antibody heavy chains and a second repertoire of antibody light chains (i.e. antibodies utilized are multimers).

For present claims 56, 59-61, 64, 78-85, and 118-119, Dower et al. teach methods of screening single-chain polypeptides for binding comprising producing a library of antibody light chains and a library of antibody heavy chains, combining the heavy and light chains and screening for antigen binding wherein the antibody heavy and light chains are produced via phage display utilizing bacteria cells for propagation and the heavy and light chains can be expressed by the same phage or different phage (i.e. in situ production; please refer to the entire specification particularly columns 3-5, 14-15; claims 1-17).

However, Feldstein et al. nor Dower et al. teach single chain polypeptides comprising both a VH and VL (i.e. scFv) or dAb (i.e. specifically, VH and VL are taught by Dower et al.).

For present claims 56, 58-61, 78-86, and 118-119, McCafferty et al. teach methods of screening libraries of scFv and dAb for binding utilizing phage display (please refer to the entire specification particularly Figure 1; column 11; Examples 1-48).

The claims would have been obvious because the substitution of one known element (i.e. antibody; multimer taught by Feldstein et al.) for another (i.e. separate VH and VL, scFv, or dAb taught by Dower et al. and/or McCafferty et al.; utilization of scFv in sandwich assay taught by Feldstein et al.) would have yielded predictable results (i.e. VH-VL binding, antibody-antigen binding, etc.) to one of ordinary skill in the art at the time of the invention. See *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007).

Arguments and Response

8. Applicants' arguments directed to the rejection under 35 USC 103 (a) as being unpatentable over Feldstein et al., Dower et al., and McCafferty et al. for claims 56, 58-67, 78-86, and 118-119 were considered but are not persuasive for the following reasons.

Applicants contend that the amendments received on December 11, 2009 negate the rejection and that a rational is not provided for combining the references. In addition, applicants contend that Feldstein et al. do not teach a repertoire of heavy chains and a repertoire of light chains and that Dower et al. and McCafferty et al. are in a different field than Feldstein et al.

Applicants' arguments are not convincing since the teachings of Feldstein et al., Dower et al., and McCafferty et al. render the method of the instant claims *prima facie* obvious.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In response to applicant's argument that Feldstein et al. is nonanalogous art with Dower et al. and McCafferty et al. and that Feldstein et al., Dower et al., and McCafferty et al. is nonanalogous art with the presently claimed invention, it has been held that a prior art reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). In this case, Feldstein et al., Dower et al., McCafferty et al., and the presently claimed invention are drawn to the "supergenus" of screening assays and the "subgenus" of antibody-antigen screening.

Feldstein et al. teach utilizing a waveguide device for antibody screening wherein continuous lines (i.e. rows of channels of waveguide device perpendicular or overlapping other rows of channels of the waveguide device) are utilized to bring antibodies (see column 4

description for Figures 7a, 7b, 8a, and 8b and columns 10, 12, 13 for example) and antigens (see column 6, lines 37-44 for example) into contact (i.e. see the entire reference particularly the Figures and columns 4-6, 9-10, 12-13; claims 1, 7). Dower et al. teaches forming antibodies by contacting various VH with various VL and then screening the antibody for antigen binding (please refer to the entire reference particularly columns 8-10). McCafferty et al. teach dAbs (please refer to the entire specification particularly Figure 1; column 11). Therefore, Dower et al. is being utilized to show that the prior art taught production of antibodies via association of various VH with various VL to produce a library which can subsequently be screened and McCafferty et al. is being utilized to show that the prior art taught dAbs.

The claims would have been obvious because the substitution of one known element (i.e. antibody; multimer taught by Feldstein et al.) for another (i.e. separate VH and VL, scFv, or dAb taught by Dower et al. and/or McCafferty et al.; utilization of scFv in sandwich assay taught by Feldstein et al.) would have yielded predictable results (i.e. VH-VL binding, antibody-antigen binding, etc.) to one of ordinary skill in the art at the time of the invention. See *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007).

9. Claims 56, 58-67, 78-86, and 118-119 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rowe et al. Anal. Chem. 71(2): 433-439, 1999 (supplied by applicants in IDS); Stevens et al. U.S. Patent 6,485,943 filed March 22, 1999; and McCafferty et al. U.S. Patent 5,969,108 issued October 19, 1999.

For present claims 56, 62-67, and 86, Rowe et al. teach methods of producing two-chain or three-chain polypeptides comprising utilizing an array immunosensor wherein vertical

channels comprise antibodies and adding samples flowed through horizontal channels (first repertoire and/or second repertoire) wherein the vertical and horizontal channels are at 90° angles wherein all members interact with each other since each channel is in contact with the other channels (e.g. all reagents in channel A interact with each of channels 1-4, see Figure 1; please refer to entire reference particularly Figure 1; experimental section).

However, Rowe et al. does not specifically teach utilizing VH or VL in separate channels (i.e. multimer antibodies are utilized).

For present claims 59-61, Stevens et al. teach methods of making recombinant antibody subunit dimers including VH-VH and VL-VL and screening against antigen comprising providing VH and/or VL and interacting the VH and/or VL (please refer to entire specification particularly abstract; column 4, lines 44-67; column 5, lines 1-9; column 6, lines 20-41; column 7, lines 23-36; columns 9-10).

However, neither Rowe et al. nor Stevens et al. teach dAb (i.e. specifically, VH and VL are taught by Stevens et al.) or phage display.

For present claims 58-61, 78-86, and 118-119, McCafferty et al. teach methods of screening libraries of scFv and dAb for binding utilizing phage display and propagation in bacterial cells (please refer to the entire specification particularly Figure 1; column 11; Examples 1-48).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of producing two-chain or three-chain polypeptides comprising utilizing an array immunosensor taught by Rowe et al. with the VH-VH or VL-VL taught by Stevens et al. and the dAb and phage display taught by McCafferty et al.

One having ordinary skill in the art would have been motivated to do this because Rowe et al. teach that immunosensors are easy to use, provide rapid assay times, have sensitivity comparable to ELISA, and can be utilized to study multianalyte binding (please refer to introduction and conclusion sections). In addition, Stevens et al. teach homologous dimerization of antibody subunits and altering amino acid sequences in the interfacial segments to improve yields of Fab and Fv products and studying the interactions via dimerization assays/screens (please refer to columns 4-5).

One of ordinary skill in the art would have had a reasonable expectation of success in the modification of the method of producing two-chain or three-chain polypeptides comprising utilizing an array immunosensor taught by Rowe et al. with the VH-VH or VL-VL taught by Stevens et al. and the dAb and phage display taught by McCafferty et al. because Rowe et al. teach utilizing immunosensors to study multianalyte interactions (e.g. VH, VL, antigen, dimmers, trimers; please refer to conclusion).

Moreover, the claims would have been obvious because the substitution of one known element (i.e. antibodies taught by Rowe et al. and Stevens et al.) for another (i.e. antibodies displayed via phage as taught by McCafferty et al.) would have yielded predictable results (i.e. VH-VL binding, antibody-antigen binding, etc.) to one of ordinary skill in the art at the time of the invention. See *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007).

Therefore, the modification of the method of producing two-chain or three-chain polypeptides comprising utilizing an array immunosensor taught by Rowe et al. with the VH-VH or VL-VL taught by Stevens et al. and the dAb and phage display taught by McCafferty et al. render the instant claims *prima facie* obvious.

Arguments and Response

10. Applicants' arguments directed to the rejection under 35 USC 103 (a) as being unpatentable over Rowe et al., Stevens et al., and McCafferty et al. for claims 56, 58-67, 78-86, and 118-119 were considered but are not persuasive for the following reasons.

Applicants contend that the combination of Rowe et al., Stevens et al., and McCafferty et al. is unpredictable. Applicants contend that Rowe et al. relates to screening of a final product/analyte by a specific antibody and does not describe or suggest use of any repertoires of molecules. In addition, applicants contend that Stevens et al. teach methods of making recombinant antibody dimers (i.e. different from Rowe et al. because Rowe et al. teach utilizing an immunoassay using an immunosensor for detection).

Applicants' arguments are not convincing since the teachings of Rowe et al., Stevens et al., and McCafferty et al. render the method of the instant claims *prima facie* obvious.

In response to applicant's argument that Rowe et al. is nonanalogous art with Stevens et al. and McCafferty et al. and that Rowe et al., Stevens et al., and McCafferty et al. is nonanalogous art with the presently claimed invention, it has been held that a prior art reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). In this case, Rowe et al., Stevens et al., McCafferty et al., and the presently claimed invention are drawn to the "supergenus" of screening assays and the "subgenus" of antibody-antigen screening.

Rowe et al. teach antibody screening utilizing channels of a flow chamber (see the entire reference particularly Figure 1). Stevens et al. teach production of antibodies via combining various VH with various VL and then screening for antigen binding (please refer to the entire reference particularly column 4). McCafferty et al. teach dAb (please refer to the entire specification particularly Figure 1; column 11). Therefore, Stevens et al. is being utilized to show that the prior art taught production of antibodies via association of various VH with various VL to produce a library which can subsequently be screened and McCafferty et al. is being utilized to show that the prior art taught dAbs. Since VH and VL binding is predictable and antibody-antigen binding is predictable in the art, the references can be combined. Additional references regarding the predictability will be provided upon request by the applicants.

See the motivation statements in the above rejection.

Double Patenting

11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. Claims 56, 58-67, 78-86, and 118-119 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10, 12, and 14-44 of copending Application No. 10/161,145. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the present invention and the invention of U.S. application 10/161,145 are drawn to methods comprising arraying a plurality of polypeptides on a support which can be single-chain or two-chain, arraying a second plurality of polypeptides/targets on a support which can be single-chain, and juxtaposing the supports so that either two-chain or three-chain polypeptides are produced.

For present claims 56, 58-67, 78-86, and 118-119, U.S. application 10/161,145 claim immobilizing target molecules on a first support wherein the target molecules can be protein, polypeptide, amino acid, whole cell or cell extract (e.g. antigen, single-chain polypeptide, VH, VL), arraying a plurality of polypeptides on a second support wherein the polypeptides can be antibodies (e.g. VH, VL, VH-VL, VH-VH, VL-VL), juxtaposing the first and second supports wherein binding can occur (e.g. making a two-chain or three-chain polypeptide library) and phage display with propagation in bacteria (please refer to claims 1-10, 12, and 14-44).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Arguments and Response

13. Applicants' arguments directed to the rejection on the ground of nonstatutory obviousness-type double patenting as being unpatentable over 10/161,145 for claims 56, 58-67, 78-86, and 118-119 were considered but are not persuasive for the following reasons.

Applicants request that the rejection be held in abeyance.

Applicants' arguments are not convincing since the claimed invention of 10/161,145 renders obvious the method of the instant claims. In addition, while a request may be made that objections or requirements as to form not necessary to further consideration of the claims be held in abeyance until allowable subject matter is indicated, the present is a rejection and will not be held in abeyance (see MPEP § 714.02).

Future Communications

Any inquiry concerning this communication or earlier communications from the examiner should be directed to AMBER D. STEELE whose telephone number is (571)272-5538. The examiner can normally be reached on Monday through Friday 9:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Amber D. Steele/
Primary Examiner, Art Unit 1639